REMARKS

Status of the Claims

Claims 2-6, 11-15 and 20-28 were considered in the final Office action mailed on December 11, 2008. As reflected in the listing of claims beginning on page 2 of this paper, Applicants amend claims 2, 3 and 11 herein. Support for the amendments can be found throughout the specification, claims and figures as originally filed, including, for example, at least at claims 2 and 3 of the specification as originally filed. Applicants submit that no new matter is introduced by the amendments to the claims. Following entry of the amendments, claims 2-6, 11-15 and 20-28 will be pending for the Examiner's further consideration.

Rejections under 35 USC 102(b): McKillop

Claims 2-6, 11-15, 20, 21 and newly added claims 22 to 28 were rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by McKillop *et al.* (August 2001, IDS) ("McKillop"). The Office action asserts that McKillop teaches the measuring of the concentration of glycated insulin in a biological sample in which the glucose levels are within the normal range, and whether or not the glycated insulin concentration is at least 20 pmol/l.

Applicants submit that method claims 2, 3 and 11 now recite an additional step. Applicants respectfully request that this additional step be taken into account when separating the claimed methods and uses from those taught in the prior art. In particular, Applicants submit that McKillop does not teach either the step of indicating the presence of diabetes when the glycated insulin is at a concentration greater than a predetermined minimum of at least about 20 pmol/l or the step of indicating a predisposition to diabetes when the glycated insulin is at a concentration greater than a predetermined minimum of at least about 20 pmol/l.

The claimed invention is novel over McKillop by disclosing that the predetermined concentration of glycated insulin of the invention should be at least 20 pmol/l, in a sample in which glucose levels are within a normal range.

The present invention is new and inventive over McKillop by demonstrating that the concentration of glycated insulin decreases over time with disease progression, and despite blood glucose concentration increasing over time with disease progression. The present Application

demonstrates that glycated insulin levels are highest at the earliest stages of diabetes - Table 1 of the present Application shows that the three type 2 diabetes patient cohorts are segregated by duration of diabetes, namely 4.8 ±0.6, 7.1 ±0.9, and 8.5 ±1.3 years. Referring now to Applicants' Figure 1, it can be seen that plasma glucose levels and plasma glycated haemoglobin levels increase with disease duration (Figure 1B and 1A, respectively). In contrast, plasma glycated insulin levels decrease with disease duration, indicating that glycated insulin levels are highest at the earliest stages of diabetes and, thereafter, that glycated insulin levels decrease with disease duration, and despite blood glucose concentration increasing over time with disease duration. Accordingly, Applicants submit that McKillop teaches away from Applicants' claimed invention.

Taken together, Applicants respectfully submit that the present invention is neither disclosed nor suggested by McKillop. In view of the foregoing, Applicants urge reconsideration of the claims and withdrawal of the rejection of claims under 35 USC § 102(b) over McKillop.

Rejections under 35 U.S.C. § 112, First Paragraph

Claims 2-6, 11-15, 20, 21 and newly added claims 22 to 28 were rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Specifically, the Office Action asserts that it is unlikely that the claimed method could be used to effectively diagnose early diabetes or a predisposition to diabetes.

Applicants refer to the Declaration of Peter Raymond Flatt filed herewith. In Aston ob/ob mice, glucose levels are normal at 6 weeks of age, but are raised at 9 weeks of age, when compared with normal control mice. Aston ob/ob mice are, therefore, in a pre-diabetic state at 6 weeks of age. Glycated insulin levels are raised at 6 weeks of age, compared with normal control mice. At 9 weeks, glycated insulin levels, although still raised, are lower than glycated insulin levels at 6 weeks of age. The data described and illustrated in the Declaration of Peter Raymond Flatt demonstrate that glycated insulin levels are raised in the pre-diabetic state in Aston ob/ob mice. These data support Applicants' submissions that glycated insulin levels fall off after diabetes is diagnosed, so that glycated insulin levels are most raised just before and around diabetes onset. These data support the teaching of the patent specification, by showing

that the methods and uses as claimed can be used to effectively diagnose early diabetes and / or determine a predisposition to diabetes in an individual.

Applicants submit that claims 2, 3 and 11, as amended, enable one skilled in the art to make and/or use the claimed invention. Specifically, the skilled artisan is sufficiently enabled to diagnose early diabetes, or to determine prediabetes in an individual, by measuring whether the concentration of glycated insulin in a sample is at least about 20 pmol/l, without the need for undue experimentation.

In view of the foregoing, Applicants urge reconsideration of the claims and withdrawal of the rejection of the claims under 35 USC § 112, first paragraph.

CONCLUSION

In view of the foregoing remarks, Applicants respectfully request allowance of claims 2-6, 11-15 and 20-28 will be pending for the Examiner's further consideration. If the Examiner believes that a telephone conversation with Applicants' attorney would expedite allowance of this application, the Examiner is cordially invited to call the undersigned attorney.

Respectfully submitted,

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